

LISTING OF THE CLAIMS

The following Listing of the Claims replaces all prior claims in the application.

Claim 1 (Original). A transgenic non-human mammal whose genome comprises a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein 695 (APP₆₉₅) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and wherein the transgene is expressed.

Claim 2 (Original). The transgenic mammal of claim 1 wherein the mammal is a mouse.

Claim 3 (Original). The transgenic mouse of claim 2 wherein the mouse is a (C3H x C57 BL6) x C57 mouse.

Claim 4 (Original). The transgenic mouse of claim 3 wherein the heterologous APP₆₉₅ is human APP₆₉₅.

Claim 5 (Original). The transgenic mouse of claim 4 wherein the mouse displays abnormal A β deposition in its central nervous system.

Claim 6 (Previously Presented). The transgenic mouse of claim 4 wherein the animal displays an appearance of Alzheimer's Disease-related pathology by 3 months of age.

Claim 7 (Previously Presented). A mouse having the transgenic mouse of claim 4 as an ancestor, wherein the mouse comprises said transgene.

Claim 8 (Withdrawn). A transgenic non-human mammal produced by:

(a) crossing a first transgenic non-human mammal in accordance with claim 1 with a second non-human mammal having a genome comprising a second gene comprising a

nucleotide sequence operably linked to a promoter and encoding a selected protein having at least one selected mutation to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic non-human mammal having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous APP₆₉₅ polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second gene comprising a nucleotide sequence operably linked to a promoter and encoding said selected protein having at least one selected mutation and expressing both said at least one first transgene and said at least one second gene.

Claim 9 (Withdrawn). The transgenic non-human mammal of claim 8 wherein the selected protein is a presenilin and the selected mutation is an AD-related mutation.

Claim 10 (Withdrawn). The transgenic non-human mammal of claim 8 wherein the selected protein is selected from the group consisting of a low density lipoprotein receptor related gene, an α 2-macroglobulin gene and a β -secretase gene and the selected mutation is an A β processing-related mutation.

Claim 11 (Withdrawn). The transgenic non-human mammal of claim 10 wherein the mammal is a mouse.

Claim 12 (Withdrawn). A transgenic mouse produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second mouse having a genome comprising a second gene comprising a nucleotide sequence operably linked to a promoter and encoding a selected protein having at least one selected mutation to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to

least one second transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 2 polypeptide wherein the methionine residue at position 239 is substituted by valine and expressing both said first and second transgenes.

Claim 18 (Withdrawn). The transgenic mouse of claim 12 produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second transgenic mouse having a genome comprising a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the leucine residue at position 286 is substituted by valine to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein (APP) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine and at least one second transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the leucine residue at position 286 is substituted by valine and expressing both said first and second transgenes.

Claim 19 (Withdrawn). The transgenic mouse of claim 12 produced by:

(a) crossing a first transgenic mouse in accordance with claim 4 with a second transgenic mouse having a genome comprising a transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous presenilin 1 polypeptide wherein the methionine residue at position 146 is substituted by leucine and the leucine residue at position 286 is substituted by valine to produce first generation offspring; and

(b) selecting from the first generation offspring a transgenic mouse having a genome comprising at least one first transgene comprising a nucleotide sequence operably linked to a promoter and encoding a heterologous amyloid precursor protein (APP) polypeptide wherein the lysine residue at position 670 is substituted by asparagine, the methionine residue at position 671 is

